Journal of Surgery and Trauma. 2027; 15(1):39-49. https://jsurgery.bums.ac.ir

Original Article

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Evaluation of the Therapeutic Potential of Selenium Nanoparticles and Coenzyme Q10 in the Prevention of Experimental Peritoneal Adhesions: A Rat Model Study

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Received: July 10, 2026

Revised: September 19,2026

Accepted: October 10, 2026

Citation: Javdani M, Bemanizadeh MM, Khosravian P, Kouhian MJ, Moghtadaei Khorasgani E, Salimi Beni M. Evaluation of the Therapeutic Potential of Selenium Nanoparticles and Coenzyme Q10 in the Prevention of Experimental Peritoneal Adhesions: A Rat Model Study. J Surg Trauma. 2027;15(1):39-49. DOI:10.61882/jsurgtrauma.15.1.39

Abstract

Introduction: Postoperative peritoneal adhesions remain a major clinical challenge following abdominal surgery, frequently leading to intestinal obstruction, chronic pain, and infertility. Oxidative stress and inflammation are known to play central roles in the pathogenesis of adhesion formation. This study evaluated the preventive effects of selenium nanoparticles and coenzyme Q10, administered individually and in combination, in a rat model of peritoneal adhesions.

Methods: This was a randomized, controlled experimental study. Sixty male Wistar rats were divided into six groups (n = 10 per group; 5 rats per time point): Sham, Control, Solvent, SeNPs (0.2 mg/kg), CoQ10 (10 mg/kg), and Mix (SeNPs + CoQ10). Adhesions were induced using the cecal scratch model. Treatments were administered intraperitoneally for four consecutive days. On days 7 and 14, adhesion severity was assessed macroscopically, and tissue samples were collected for histopathological evaluation of inflammation, vascularization, and fibroplasia. Antioxidant enzyme activities (SOD, GPx), malondialdehyde levels, and pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) were measured. Statistical analysis was performed using SPSS, version 27.0 and one-way ANOVA, followed by Tukey's post hoc test was used for normally distributed data, whereas the Kruskal–Wallis test followed by the Mann–Whitney U test with Bonferroni correction was used for non-normally distributed data.

Results: The combination therapy significantly reduced adhesion severity compared with the control and monotherapy groups on both days 7 and 14 ($P < 0.05$). Histopathological analysis revealed that the combination group exhibited the highest fibroplasia scores (least fibrosis), which were comparable to those of the sham group. Biochemical analyses showed that the combination treatment normalized malondialdehyde levels, restored SOD and GPx activities, and significantly suppressed TNF-α, IL-1β, and IL-6 levels ($P < 0.05$), reaching levels indistinguishable from those of the sham group.

Conclusions: Co-administration of selenium nanoparticles and coenzyme Q10 exerts synergistic protection against peritoneal adhesions by enhancing antioxidant defenses and suppressing pro-inflammatory cytokines. This combination represents a promising dual-agent strategy for preventing postoperative peritoneal adhesions.

Key words: Inflammation, Oxidative Stress, Peritoneal Adhesions, Selenium Nanoparticles, Ubiquinone

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Introduction

Postoperative peritoneal adhesions are fibrotic bands that develop between abdominal organs and the peritoneal surface following surgical trauma. These adhesions affect up to 90% of patients undergoing abdominal surgery and impose a substantial clinical burden, manifesting as intestinal obstruction, chronic pelvic pain, female infertility, and increased technical difficulty in subsequent surgical procedures [1, 2]. Despite considerable advances in surgical techniques and the introduction of various barrier materials, effective prevention remains an unmet clinical need, underscoring the urgent demand for novel therapeutic strategies [3, 4].

The pathogenesis of peritoneal adhesions is a multifaceted process initiated by peritoneal injury. Surgical manipulation disrupts the mesothelial barrier, triggering an inflammatory cascade characterized by the release of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) and the extravasation of fibrin-rich exudate [5]. Under physiological conditions, this fibrin matrix is degraded by the fibrinolytic system, primarily through the activity of tissue plasminogen activator. However, peritoneal injury suppresses tissue plasminogen activator activity and upregulates plasminogen activator inhibitors (PAI-1, PAI-2), shifting the balance toward persistent fibrin deposition [6]. This persistent fibrin scaffold serves as a substrate for fibroblast infiltration, myofibroblast differentiation, and excessive collagen deposition, ultimately resulting in dense, permanent adhesions [7, 8].

Oxidative stress plays a pivotal role in this process. Surgical trauma generates reactive oxygen species through ischemia-reperfusion injury and inflammatory cell infiltration [9]. Excessive levels of reactive oxygen species deplete endogenous antioxidants, promote lipid peroxidation, activate NF-κB, and upregulate TGF-β1, a master regulator of fibrosis [10, 11]. This interconnected oxidative-inflammatory-fibrotic axis represents a critical therapeutic target for adhesion prevention [12].

Despite the individual benefits of selenium nanoparticles and coenzyme Q10, their combined effects on peritoneal adhesions remain unexplored. Given their complementary mechanisms of action, with selenium nanoparticles primarily enhancing enzymatic antioxidant defenses and coenzyme Q10 acting as a direct radical scavenger and membrane stabilizer, we hypothesized that co-administration would exert synergistic protection by simultaneously targeting oxidative stress, inflammation, and fibrosis [13]. To our knowledge, this is the first study to evaluate the preventive efficacy of this combination in a peritoneal adhesion model. Therefore, this study aimed to evaluate the preventive efficacy of selenium nanoparticles and coenzyme Q10, individually and in combination, on experimentally induced peritoneal adhesions in rats.

Methods

Animals and Experimental Design

This was a randomized, controlled experimental study. Sixty male Wistar rats (10–11 weeks, 250 ± 20 g) were obtained from the institutional animal facility and maintained under standard conditions (23 ± 2°C, 12:12-h light/dark cycle, food and water ad libitum) for one week prior to experimentation. All procedures were approved by the Institutional Animal Ethics Committee (IR.IAU.SHK.REC.1405.097) and conducted in accordance with ARRIVE guidelines [14]. All efforts were made to minimize animal suffering and reduce the number of animals used in accordance with the 3Rs principle (Replacement, Reduction, Refinement). Anesthesia and euthanasia were performed using approved methods to ensure humane treatment.

Sample size (n=5 per group per time point) was determined based on previous studies in similar experimental models of peritoneal adhesion, which demonstrated sufficient statistical power (≥80%) to detect significant differences in adhesion scores and biochemical parameters with n = 5-8 animals per group [15-17]. This sample size is consistent with published studies in the field and is sufficient for non-parametric statistical analyses. The sample size of 5 animals per group per time point was chosen to ensure adequate statistical power while minimizing animal use in accordance with the 3Rs principle.

Rats were randomly allocated into six groups (n=10 each, 5 per time point): (A) Sham (Laparotomy only); (B) Control (Adhesion induction without treatment); (C) Solvent (distilled water + Tween 80); (D) SeNPs (Selenium nanoparticles (0.2 mg/kg)); (E) CoQ10 (Coenzyme Q10 (10 mg/kg)); (F) Mix (SeNPs + CoQ10 at the same doses).

The study duration was 14 days, with animals evaluated at two time points (day 7 and day 14).

Adhesion Induction and Treatment

Briefly, under anesthesia with ketamine (70 mg/kg) and xylazine (10 mg/kg), a midline

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laparotomy was performed. The cecum was exteriorized, and its serosal surface was scratched with a sterile scalpel until petechial hemorrhages appeared. The cecum was returned to its anatomical position, and the abdomen was closed in layers using absorbable sutures [18].

Treatments were administered intraperitoneally (0.5 mL) for four consecutive days following surgery. The 4-day treatment period was selected based on previous studies demonstrating that the critical window for adhesion formation and the inflammatory response peaks within the first 3-5 days postoperatively [9, 12]. This duration has been successfully used in similar experimental models for evaluating anti-adhesion agents [8, 10]. Additionally, the intraperitoneal administration of selenium nanoparticles and coenzyme Q10 provides sustained local effects, with previous pharmacokinetic studies showing that selenium nanoparticles remain detectable in peritoneal tissues for up to 72 hours post-administration [19]. This short treatment protocol was chosen to target the early inflammatory phase while minimizing potential systemic toxicity and animal stress associated with prolonged daily injections. On days 7 and 14, five rats per group were euthanized using an anesthetic overdose for tissue collection [15].

Adhesion Scoring and Histopathology

Histopathological evaluation scored inflammation, vascularization, and fibroplasia on a 0–5 scale by a blinded observer [17]. Histopathological evaluation of inflammation, vascularization, and fibroplasia was performed by a blinded observer using a 0–5 scale, where higher scores indicated better outcomes (less pathology), as follows: (A) Inflammation: 0 = very extensive, 1 = extensive, 2 = severe, 3 = moderate, 4 = mild, 5 = none; (B) Vascularization: 0 = abundant, 1 = marked, 2 = moderate, 3 = mild, 4 = minimal, 5 = none; (C) Fibroplasia: 0 = extensive, 1 = marked, 2 = moderate, 3 = mild, 4 = minimal, 5 = none.

Biochemical Analyses

Cecal tissue was homogenized in phosphate buffer. Superoxide dismutase and glutathione peroxidase activities, malondialdehyde levels, and pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) were measured using commercial ELISA kits (Navand Salamat Co., Iran) according to the manufacturer's instructions [20, 21].

Statistical Analysis

Statistical analysis was performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Normality of data distribution was assessed using the Shapiro-Wilk test ($P > 0.05$ considered normally distributed). Homogeneity of variances was evaluated using Levene's test. For normally distributed data with homogeneous variances, one-way ANOVA was used followed by Tukey's post-hoc test. For non-normally distributed data, the Kruskal-Wallis test was used, followed by the Mann-Whitney U test with Bonferroni correction for pairwise comparisons. Histopathological data were analyzed using non-parametric tests. A P-value of less than 0.05 was considered statistically significant. Results are presented as mean ± SD or median (min-max).

Results

Macroscopic Adhesion Scores

On day 7, adhesion scores differed significantly among groups ($P < 0.001$). The control and solvent groups exhibited severe adhesions, while all treatment groups (selenium nanoparticles, coenzyme Q10, and combination) showed significantly lower scores ($P < 0.001$). The combination group demonstrated significantly fewer adhesions than both monotherapy groups ($P < 0.05$), suggesting a synergistic effect (Figure 1).

On day 14, the combination group maintained significantly lower adhesion grades compared to selenium nanoparticles and coenzyme Q10 alone ($P = 0.031$). The control and solvent groups continued to show severe adhesions, whereas the sham group consistently exhibited minimal adhesion formation (Figure 2).

Histopathological Findings

Adhesion severity was assessed macroscopically using a validated five-grade scoring system (5 = no adhesion, 1 = most severe) [22]. Tissue samples were fixed in 10% formalin, processed, sectioned (5 μm), and stained with hematoxylin and eosin. On day 7, the combination and sham groups exhibited the highest fibroplasia scores (indicating the least fibrosis), significantly outperforming the control and solvent groups ($P = 0.009–0.016$). Inflammation scores were highest in the sham group, with the combination and coenzyme Q10 groups showing significant improvement over the control group ($P = 0.009–0.037$). Vascularization scores were lowest in the sham group ($P = 0.009$), with no significant differences observed among the other groups ($P = 0.009$) (Table 1 and Figure 3).

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Table 1. Median (min-max) scores for inflammation, vascularization, and fibroplasia on day 7.

Group	Inflammation	Vascularization	Fibroplasia
Control	2 (2-3)[a] Q1=2 Q3=3	4 (3-4)[a] Q1=4 Q2=4	3 (3-4)[a,b] Q1=3 Q2=3
Sham	5 (4-5)[b] Q1=5 Q3=5	2 (2-3)[b] Q1=2 Q2=2	5 (4-5)[c] Q1=4 Q2=5
Solvent	3 (2-3)[a] Q1=2 Q3=3	4 (3-4)[a] Q1=4 Q2=4	2 (2-4)[a] Q1=2 Q2=3
SeNPs	3 (3-4)[a] Q1=3 Q3=4	3 (3-4)[c] Q1=4 Q2=4	4 (2-4)[b] Q1=3 Q2=4
CoQ10	4 (3-4)[c] Q1=3 Q3=4	3 (3-4)[c] Q1=3 Q2=4	4 (2-4)[b] Q1=4 Q2=4
Mix	4 (3-5)[c] Q1=4 Q3=5	4 (3-4)[a] Q1=3 Q2=4	5 (4-5)[c] Q1=4 Q2=5
P-value	0.003	0.009	0.026

Note: Different superscript letters within each column indicate significant differences between groups ($P < 0.05$, Mann-Whitney U test). Groups sharing the same letter are not significantly different. All parameters were scored on a scale of 0–5, with higher scores indicating better outcomes (less inflammation, less vascularization, and less fibroplasia).

On day 14, the combination and sham groups maintained the highest fibroplasia scores, significantly better than the control, solvent, and selenium nanoparticle groups ($P = 0.009–0.032$). Inflammation was similar across all groups by day 14 ($P = 0.447$). Vascularization was highest in the control and selenium nanoparticle groups, while the sham, coenzyme Q10, and combination groups showed moderate levels ($P = 0.005$) (Table 2 and Figure 4).

Oxidative Stress Markers

On day 7, superoxide dismutase activity was significantly reduced in the control group compared to the sham group ($P < 0.05$), while the combination group showed no significant difference from the sham group. The combination group showed a 60.2% reduction in MDA levels compared to the control group (from 5.9 ± 2.1 to 2.4 ± 0.97 nmol/mg protein), and a 15.8% increase in SOD activity compared to the control group. Malondialdehyde levels were significantly elevated in the control group (5.9 ± 2.1) compared to the sham group (0.92 ± 0.49) and all treatment groups ($P < 0.05$). Glutathione peroxidase activity was lowest in the control group (21.28 ± 8.45) and highest in the sham group (43.34 ± 6.9) (Table 3).

Table 2. Median (min-max) scores for inflammation, vascularization, and fibroplasia on day 14.

Group	Inflammation	Vascularization	Fibroplasia
Control	5 (4-5)[a] Q1=4 Q2=5	5 (4-5)[a] Q1=4 Q2=5	3 (3-4)[a,b] Q1=3 Q2=3
Sham	5 (5-5)[a] Q1=5 Q2=5	3 (2-3)[b] Q1=3 Q2=3	5 (4-5)[c] Q1=4 Q2=5
Solvent	5 (4-5)[a] Q1=4 Q2=5	4 (3-4)[c] Q1=4 Q2=4	3 (3-4)[a,b] Q1=3 Q2=3
SeNPs	5 (4-5)[a] Q1=5 Q2=5	5 (4-5)[a] Q1=5 Q2=5	3 (2-4)[a] Q1=3 Q2=4
CoQ10	5 (4-5)[a] Q1=5 Q2=5	3 (3-4)[b] Q1=3 Q2=4	4 (2-4)[b] Q1=4 Q2=4
Mix	5 (5-5)[a] Q1=5 Q2=5	3 (2-4)[b] Q1=2 Q2=4	5 (4-5)[c] Q1=4 Q2=5
P-value	0.447	0.005	0.016

Note: Different superscript letters within each column indicate significant differences ($P < 0.05$, Mann-Whitney U test). Groups with the same letter are not significantly different. All parameters were scored on a scale of 0–5, with higher scores indicating better outcomes. All parameters were scored on a scale of 0–5, with higher scores indicating better outcomes (less inflammation, less vascularization, and less fibroplasia).

Table 3. Comparison of antioxidant enzyme activities on day 7.

Group	SOD (U/mg protein)	MDA (nmol/mg protein)	GPx (U/mg protein)
Sham	93.8 ± 17.83[a]	0.92 ± 0.49[a]	43.34 ± 6.9[a]
Control	34.92 ± 11.58[b]	5.9 ± 2.1[b]	21.28 ± 8.45[b]
Solvent	44.46 ± 14.14[b]	4.3 ± 1.48[b,c]	25.32 ± 8.85[a,b]
SeNPs	50.69 ± 16.47[b]	3.06 ± 1.13[c]	37.58±17.11[a,b]
CoQ10	46.48 ± 14.07[b]	3.06 ± 1.27[c]	37.86±14.02[a,b]
Mix	65.28±24.06[a,b]	2.4 ± 0.97[c]	39.22±16.2[a,b]

Note: Data are presented as mean ± SD (n = 5 per group). Different superscript letters indicate significant differences within each column ($P < 0.05$).

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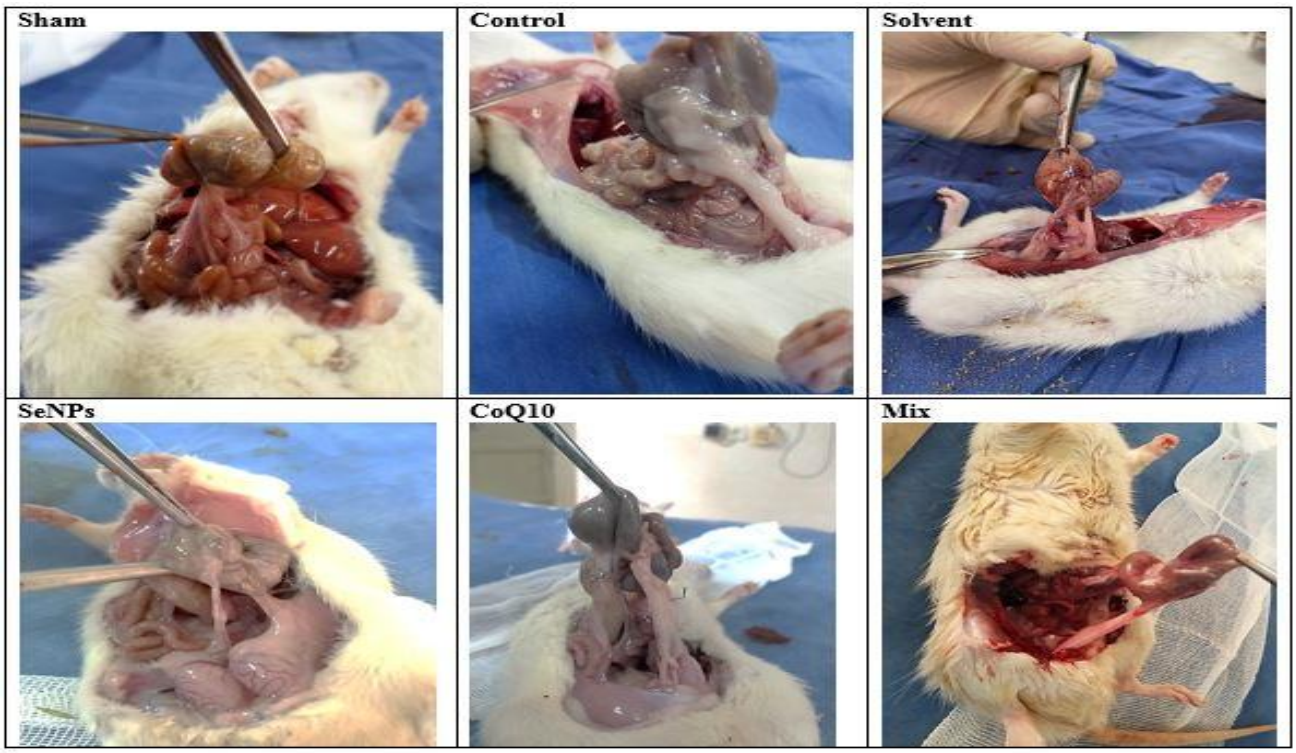


Figure 1. Comparison of gross adhesion grades among the study groups on day 7.

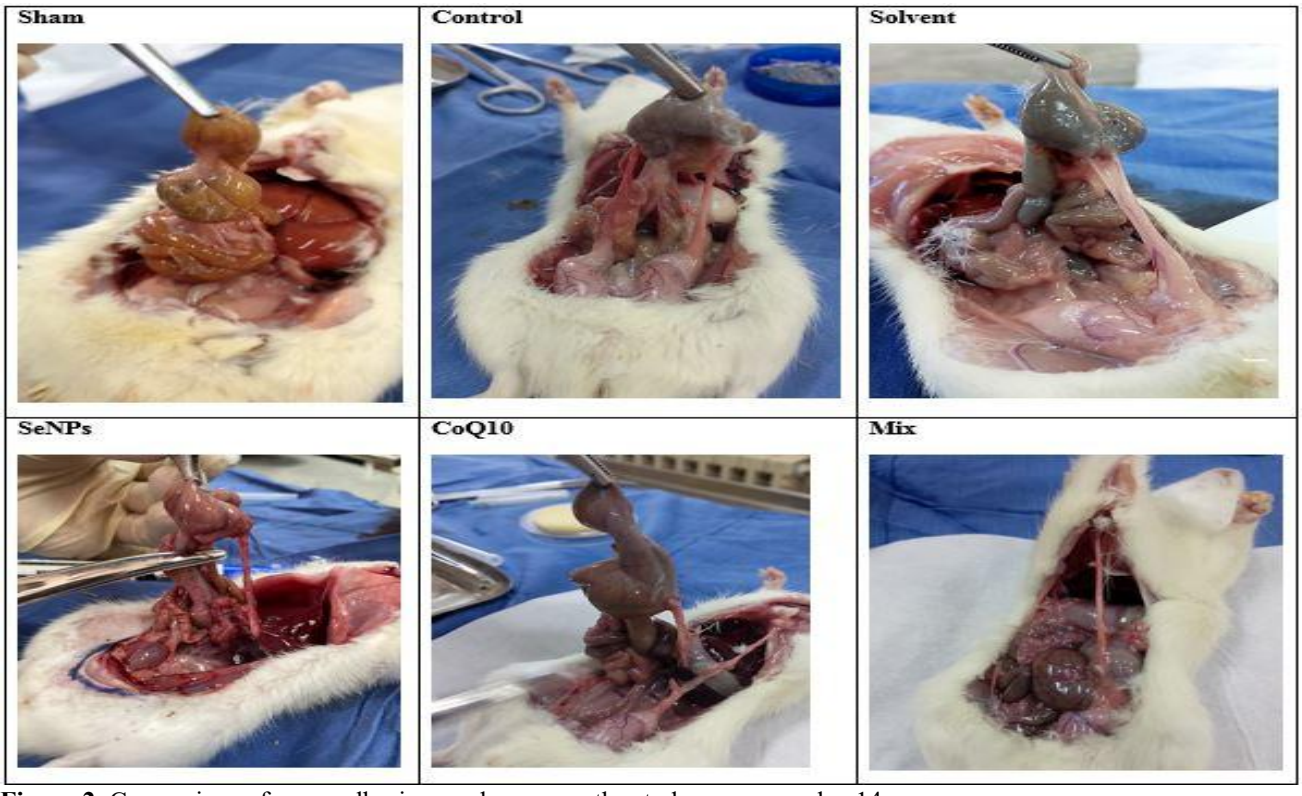


Figure 2. Comparison of gross adhesion grades among the study groups on day 14.

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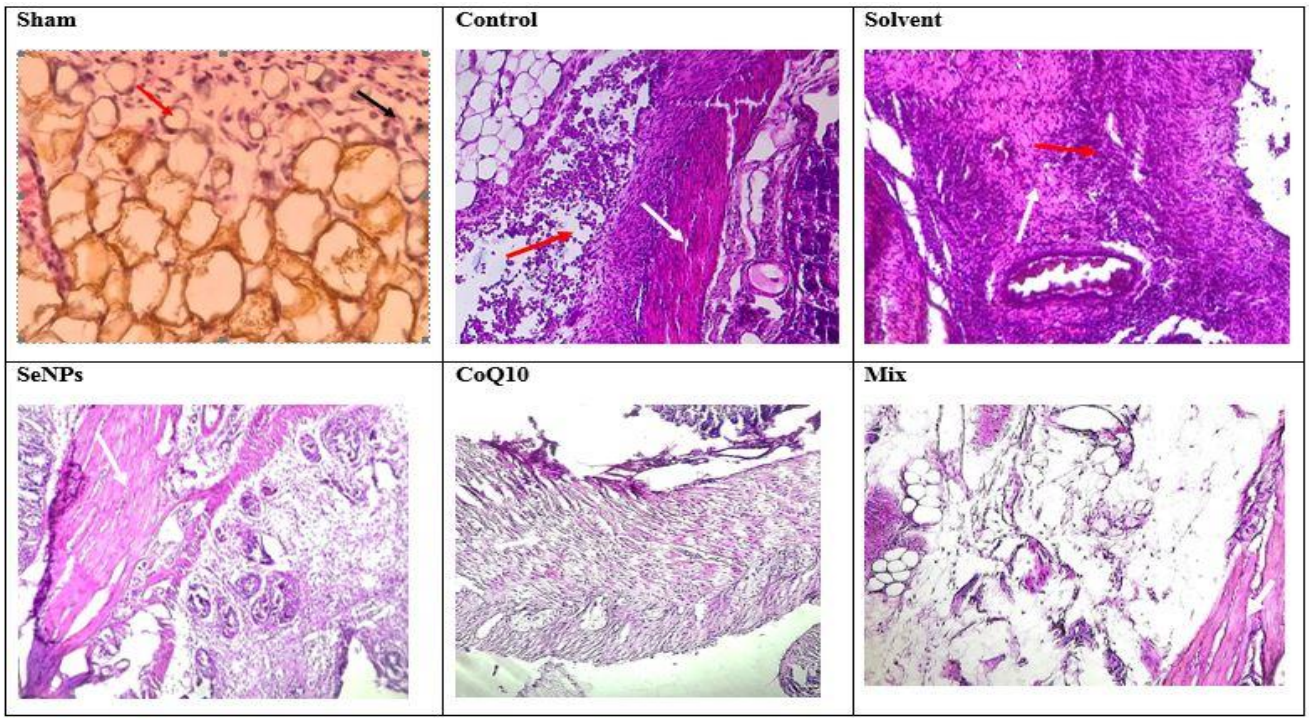


Figure 3. Microscopic findings in different groups on day 7 (H&E staining; original magnification, ×100). Sham group: Delicate connective tissue fibers (black arrow) and newly formed blood vessels (red arrow). Control group: Dense collagen fiber formation (white arrow) and inflammation (red arrow); Solvent group: Dense connective tissue formation (white arrows), hyperemia (black arrow), and inflammation (red arrow); SeNPs group: Moderately dense connective tissue fibers at the lesion site (white arrow); CoQ10 group: Moderately dense connective tissue at the site (white arrow); Mix group: Presence of thin connective tissue fibers at the site (white arrow).

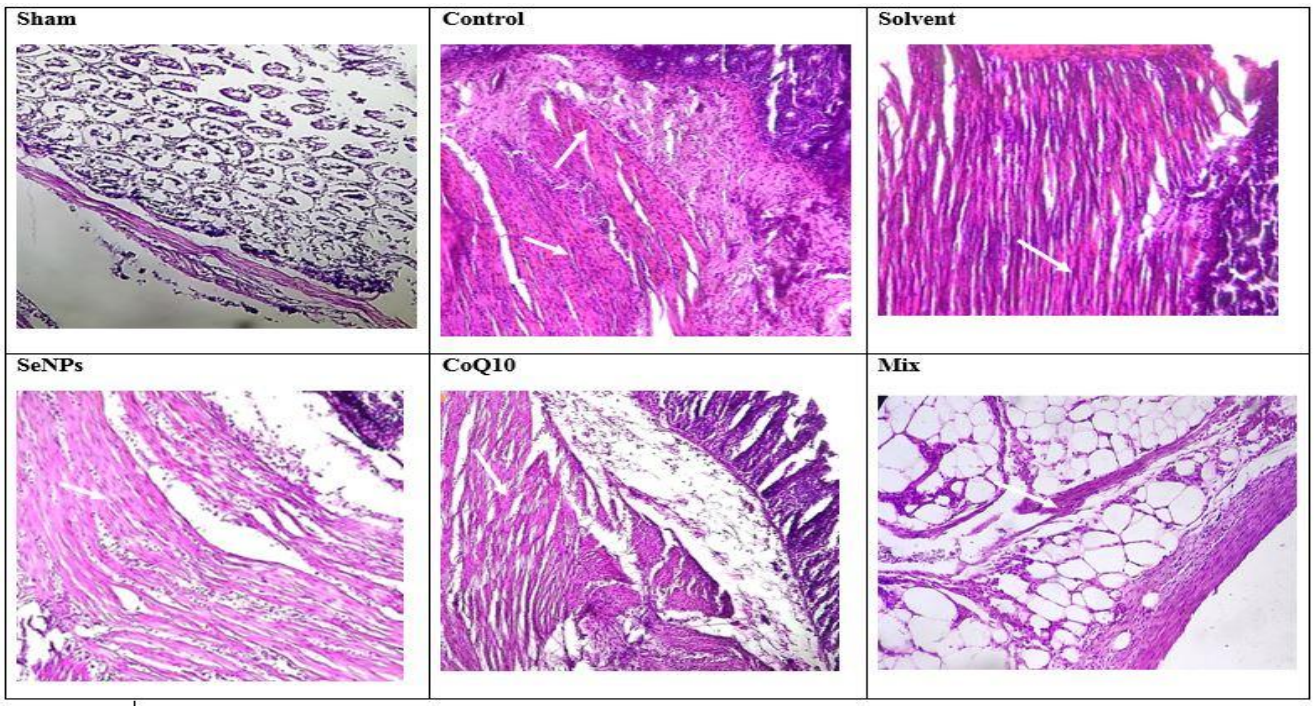


Figure 4. Microscopic findings in different groups on day 14 (H&E staining; original magnification, ×100). Sham group: Absence of adhesion; Control group: High deposition of collagen fibers (white arrows); Solvent group: Presence of connective tissue fibers at the lesion site (white arrow); SeNPs group: Presence of dense connective tissue and adhesions at the site (white arrows); CoQ10 group: Moderately dense connective tissue and adhesion formation (white arrow); Mix group: Presence of loose connective tissue fibers at the site (white arrow).

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On day 14, superoxide dismutase activity was restored in all treatment groups to levels near those of the sham group. Malondialdehyde levels remained elevated in the control group (5.1 ± 2.18) compared to the sham group (1.00 ± 0.43) and the combination group (2.08 ± 1.27) ($P < 0.05$). Glutathione peroxidase activity was significantly increased in the selenium nanoparticle and coenzyme Q10 groups compared to the control group ($P = 0.014$ and $P = 0.028$, respectively), with the combination group showing a trend toward improvement ($P = 0.065$) (Table 4).

Table 4. Comparison of antioxidant enzyme activities on day 14.

Group	SOD (U/mg protein)	MDA (nmol/mg protein)	GPx (U/mg protein)
Sham	93.22 ± 21.00[a]	1.00 ± 0.43[a]	47.3±11.96[a]
Control	51.38 ± 10.78[b]	5.1 ± 2.18[b]	22.92 ± 6.14[b]
Solvent	62.28±12.85[ab]	3.38 ± 1.45[ab]	33.44±10.87[ab]
SeNPs	79.92±17.29[ab]	2.78 ± 1.03[ab]	49.32 ±12.8[a]
CoQ10	85.16±18.43[ab]	2.6 ± 0.98[ab]	47.14 ±13.82[a]
Mix	72.12±18.16[ab]	2.08 ± 1.27[a]	44.32 ±11.17[a]

Note: Data are presented as mean ± SD (n = 5 per group). Different superscript letters indicate significant differences within each column ($P < 0.05$).

Cytokine Levels

On day 7, TNF-α, IL-1β, and IL-6 were significantly elevated in the control group compared to the sham group ($P = 0.013$, $P = 0.003$, $P = 0.001$, respectively). The combination group effectively reduced all three cytokines to levels indistinguishable from those of the sham group, demonstrating superior anti-inflammatory efficacy compared to monotherapies (Table 5).

Table 5. Comparison of pro-inflammatory cytokine levels on day 7.

Group	TNF-α(pg/mL)	IL-1β (pg/mL)	IL-6 (pg/mL)
Sham	41.82 ± 20.16[a]	39.54 ±16.34[a]	25.34±11.06[a]
Control	142.26±68.39[b]	95.68±25.95[b]	103.28±35.64[b]
Solvent	94.30±47.39[ab]	70.74±21.83[ab]	82.14±28.68[ab]
SeNPs	83.06±41.90[ab]	54.72±14.45[a]	54.02±23.67[a]
CoQ10	78.82±43.69[ab]	58.40±19.29[ab]	53.98 ± 25.39[a]
Mix	47.58 ± 51.60[a]	53.46±23.87[a]	44.10 ± 15.95[a]

Note: Data are presented as mean ± SD (n = 5 per group). Different superscript letters indicate significant differences within each column ($P < 0.05$).

On day 14, TNF-α and IL-1β levels converged across all groups. However, IL-6 remained significantly elevated in the control group (66.20 ± 18.61) compared to the sham group (25.88 ± 11.38) and the combination group (28.72 ± 8.51) ($P = 0.001$ and $P = 0.002$, respectively), indicating persistent inflammation in untreated animals (Table 6).

Table 6. Comparison of pro-inflammatory cytokine levels on day 14.

Group	TNF-α (pg/mL)	IL-1β (pg/mL)	IL-6 (pg/mL)
Sham	43.08 ±22.39[a]	41.88 ±16.79[a]	25.88 ± 11.38[a]
Control	82.02 ± 40.17[a]	73.38 ±29.48[a]	66.20 ± 18.61[b]
Solvent	60.34 ± 29.95[a]	50.44 ±21.67[a]	44.56±13.77[ab]
SeNPs	62.64 ± 23.96[a]	40.94 ±12.27[a]	48.60±10.78[ab]
CoQ10	64.14 ± 25.21[a]	40.00 ±16.03[a]	47.00±14.82[ab]
Mix	40.34 ± 13.68[a]	47.36 ±10.80[a]	28.72 ±8.51[a]

Note: Data are presented as mean ± SD (n = 5 per group). Different superscript letters indicate significant differences within each column ($P < 0.05$).

Discussion

The present study provides evidence that co-administration of selenium nanoparticles and coenzyme Q10 exerts synergistic protective effects against postoperative peritoneal adhesions in a rat model. The combination therapy significantly reduced adhesion severity, attenuated oxidative stress, suppressed pro-inflammatory cytokines, and mitigated fibrosis compared with either monotherapy. The significant reduction in adhesion scores observed in the combination group (median: 4, range: 3-5 on day 14) compared with the control group (median: 2, range: 2-3) demonstrates the enhanced protective effect of combined therapy. This finding is consistent with the biochemical results showing complete normalization of inflammatory cytokines and restoration of antioxidant enzyme activities. These findings highlight the potential of this dual-agent approach for adhesion prevention [23].

Although we did not directly measure TGF-β1 protein expression or NF-κB activation in this study, the observed suppression of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) and the higher fibroplasia scores (indicating reduced fibrosis) are consistent with previously reported mechanisms of action. Previous studies have demonstrated that selenium nanoparticles suppress TGF-β1/Smad signaling and inhibit NF-κB activation, while coenzyme Q10 similarly modulates these pathways [22, 24]. However, we acknowledge that direct

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immunohistochemical or immunoblotting analyses would be required to confirm these mechanistic inferences. The superior efficacy of the combination can be attributed to the complementary mechanisms of selenium nanoparticles and coenzyme Q10.

The antioxidant and broader biomedical potential of selenium-based nanoparticles has also been highlighted in previous reviews, supporting their investigation as potential therapeutic agents in oxidative stress-related conditions [25]. Selenium nanoparticles enhance endogenous antioxidant defenses by serving as a cofactor for glutathione peroxidase, directly scavenging reactive oxygen species, and modulating NF-κB and TGF-β1/Smad signaling [19, 24]. Coenzyme Q10, as a mitochondrial electron carrier, stabilizes cell membranes, regenerates other antioxidants (including vitamin E), and similarly suppresses NF-κB activation and TGF-β1-mediated fibrosis [22, 26]. Their combined action likely produces more comprehensive and sustained modulation of the oxidative-inflammatory-fibrotic axis [13].

Our findings align with previous reports demonstrating the individual anti-adhesive potential of these agents. Kuşaslan et al. reported that coenzyme Q10 (30 mg/kg) significantly reduced adhesion scores and improved histopathological parameters in rats [22]. Historically, different pharmacological strategies have been investigated to prevent postoperative intraperitoneal adhesions, including the use of proteolytic enzymes, reflecting the longstanding interest in modifying the biological processes involved in adhesion formation [27]. Shirian et al. demonstrated that selenium nanoparticles combined with tannic acid effectively reduced peritoneal adhesions through antioxidant and anti-inflammatory mechanisms [8]. However, our study extends these observations by demonstrating that the combination of selenium nanoparticles and coenzyme Q10 produces synergistic effects exceeding those of either agent alone.

Oxidative stress is a critical driver of peritoneal adhesion pathogenesis [9]. Surgical manipulation generates reactive oxygen species that deplete antioxidants, promote lipid peroxidation, and activate pro-inflammatory and pro-fibrotic signaling pathways [10, 11]. Our biochemical analyses confirmed that the control group exhibited significantly elevated malondialdehyde and reduced superoxide dismutase and glutathione peroxidase activities. Importantly, all treatment regimens normalized malondialdehyde levels, with the combination group showing the most consistent restoration of antioxidant enzyme activities across both time points. This sustained antioxidant protection likely contributes to the enhanced anti-adhesive efficacy of the combination.

Pro-inflammatory cytokines, particularly TNF-α, IL-1β, and IL-6, play central roles in adhesion formation by promoting leukocyte recruitment, fibroblast proliferation, and fibrin deposition [5, 6]. The combination group demonstrated exceptional anti-inflammatory efficacy, reducing all three cytokines to levels indistinguishable from the sham group on day 7 and maintaining IL-6 suppression through day 14. This complete normalization of the inflammatory response was not consistently achieved by monotherapies, underscoring the synergistic benefit of combined therapy.

The anti-fibrotic effects observed in the combination group are particularly noteworthy. Fibroplasia scores in the combination group were comparable to the sham group on both days 7 and 14, despite only moderate vascularization. This dissociation suggests that the combination reduces fibrosis through mechanisms partially independent of angiogenesis, possibly via direct inhibition of fibroblast activation or TGF-β1/Smad signaling [22, 24]. Previous studies have demonstrated that selenium nanoparticles suppress TGF-β1-induced fibroblast-to-myofibroblast differentiation and collagen production, while coenzyme Q10 reduces collagen I and III synthesis in experimental adhesion models [13].

Several limitations warrant consideration. First, the sample size (n=5 per time point) is relatively small and may limit generalizability. Second, molecular-level analyses (e.g., immunohistochemistry for TGF-β1, Smad proteins, α-SMA) were not performed, which would have provided direct evidence for the proposed mechanisms [7]. Third, the 14-day study duration may not capture long-term outcomes, including adhesion reformation. Fourth, systemic toxicity and pharmacokinetics of repeated nanoparticle administration were not assessed. Fifth, the translational relevance of rodent adhesion models to human clinical scenarios, while well-established, may not fully recapitulate the complexity of postoperative adhesion formation in patients with comorbidities [28].

Future studies should focus on the following: (1) elucidating the detailed molecular mechanisms, particularly regarding TGF-β1/Smad signaling and myofibroblast differentiation, using specific

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immunohistochemical and immunoblotting techniques; (2) evaluating the safety and pharmacokinetics of repeated selenium nanoparticle and coenzyme Q10 administration; (3) optimizing the formulation and dosing regimen for potential clinical translation; (4) validating these promising results in larger animal models; and (5) investigating the potential of this combination in preventing adhesion reformation following adhesiolysis [29, 30].

Conclusions

In conclusion, this study demonstrates that co-administration of selenium nanoparticles and coenzyme Q10 significantly reduces peritoneal adhesion severity, attenuates oxidative stress, suppresses pro-inflammatory cytokines, and mitigates fibrosis in a rat model. The combination therapy showed superior efficacy compared to either monotherapy alone at both time points evaluated. The ability of the combination therapy to completely normalize inflammatory markers to sham levels, maintain antioxidant capacity, and consistently reduce fibroplasia underscores the potential of combined selenium nanoparticles and coenzyme Q10 as a promising strategy for preventing postoperative peritoneal adhesions. These findings support further investigation of this combination for postoperative adhesion prevention.

Ethics Approval and Consent to Participate

All procedures were approved by the Institutional Animal Ethics Committee (IR.IAU.SHK.REC.1405.097) and conducted in accordance with ARRIVE guidelines [14]. Animals were housed under standard conditions with free access to food and water. All efforts were made to minimize animal suffering and reduce the number of animals used in accordance with the 3Rs principle (Replacement, Reduction, Refinement). Anesthesia and euthanasia were performed using approved methods to ensure humane treatment.

Consent for Publication

Not applicable.

Data Availability Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Funding Statement

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Acknowledgements

The authors would like to thank the personnel of the institutional animal facility for their technical assistance.

Authors' Contribution

MJ conceived the study, developed the methodology, conducted the investigation, and drafted the original manuscript. PK contributed to the study conception and interpretation of the findings. MMB and MJK contributed to proposal preparation and data collection. EMK performed data curation and formal analysis. MSB coordinated the study and contributed to data collection. All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work.

Conflict of Interest

The authors declare no competing interests.

Declaration of Generative Artificial Intelligence (AI) in Scientific Writing

During the preparation of this manuscript, AI tools (ChatGPT [OpenAI, https://chatgpt.com]) were used solely for language polishing and grammatical refinement; no AI was used for data collection, analysis, interpretation, or scientific content generation, and all authors take full responsibility for the final content.

References

1. Brüggmann D, Tchartchian G, Wallwiener M, Münstedt K, Tinneberg HR, Hackethal A. Intra-abdominal adhesions: definition, origin, significance in surgical practice, and treatment options. Dtsch Arztebl Int. 2010;107(44):769-75. [DOI: 10.3238/arztebl.2010.0769]
2. Hassanabad AF, Zarzycki AN, Jeon K, Dundas JA, Vasanthan V, Deniset JF, et al. Prevention of Post-Operative Adhesions: A Comprehensive Review of Present and Emerging Strategies. Biomolecules. 2021;11(7):1027. [DOI: 10.3390/biom11071027]
3. Moris D, Chakedis J, Rahnemai-Azar AA, Wilson A, Hennessy MM, Athanasiou A, et al. Postoperative abdominal adhesions: clinical significance and advances in prevention and management. J Gastrointest Surg. 2017;21(10):1713-22. [DOI: 10.1007/s11605-017-3488-9]

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4. Liao J, Li X, Fan Y. Prevention strategies of postoperative adhesion in soft tissues by applying biomaterials: Based on the mechanisms of occurrence and development of adhesions. Bioact Mater. 2023;26:387-412. [DOI: 10.1016/j.bioactmat.2023.02.026]
5. Holmdahl LE, Al-Jabreen, Risberg B. The role of fibrinolysis in the formation of peritoneal adhesions. Wound Repair Regen. 1994;2(3):171-76. [DOI: 10.1046/j.1524-475X.1994.20306.x]
6. Hellebrekers BW, Trimbos-Kemper TC, Trimbos JB, Emeis JJ, Kooistra. Use of fibrinolytic agents in the prevention of postoperative adhesion formation. Fertil Steril. 2000;74(2):203-12. [DOI: 10.1016/S0015-0282(00)00656-7]
7. Chegini N. Peritoneal molecular environment, adhesion formation and clinical implication. Front Biosci. 2002;7(16):91-115. [DOI: 10.2741/a911]
8. Shirian S, Emamjomehzadeh PS, Javdani M, Khosravian P, Karimi B. Investigating the therapeutic effects of selenium nanoparticles and tannic acid on postoperative peritoneal adhesion in rats. J Surg Trauma. 2025;13(4):144-53. [DOI: 10.61882/jsurgtrauma.13.4.144]
9. Reed KL, Heydrick SJ, Aarons CB, Prushik S, Gower AC, Stucchi AF, et al. A neurokinin-1 receptor antagonist that reduces intra-abdominal adhesion formation decreases oxidative stress in the peritoneum. Am J Physiol Gastrointest Liver Physiol. 2007;293(3):544-51. [DOI: 10.1152/ajpgi.00226.2007]
10. Kaboutari J, Ghorbani M, Karimi B, Javdani M, Khosraviyan P. Effects of the slow-release curcumin-loaded selenium nanoparticles on experimental peritonitis. Iran J Vet Med. 2024;18(4):555-66. [DOI: 10.32598/IJVM.18.4.1005255]
11. Andrés CMC, Pérez de la Lastra JM, Munguira EB, Juan CA, Pérez-Lebeña E. Selenium nanoparticles in critical illness—anti-inflammatory and antioxidant effects. Dietetics. 2025;4(1):6. [DOI: 10.3390/dietetics4010006]
12. Brochhausen C, Schmitt VH, Planck CN, Rajab TK, Hollemann D, Tapprich C, et al. Current strategies and future perspectives for intraperitoneal adhesion prevention. J Gastrointest Surg. 2012;16(6):1256-74. [DOI: 10.1007/s11605-011-1819-9]
13. Deng X, Zheng C, Wang S, Yang R, Liu Z, Chen T. Treatment with a probiotic combination reduces abdominal adhesion in rats by decreasing intestinal inflammation and restoring microbial composition. Oncol Rep. 2020;43(3):986-98. [DOI: 10.3892/or.2020.7463]
14. Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG. Improving bioscience research reporting: the ARRIVE guidelines for reporting animal research. PLoS Biol. 2010;8(6):e1000412. [DOI: 10.1371/journal.pbio.1000412]
15. Bozdag Z, Gumus M, Arıkanoglu Z, Ibiloglu I, Kaya S, Evliyaoglu O. Effect of intraperitoneal thymoquinone on postoperative peritoneal adhesions. Acta Chir Belg. 2015;115(5):364-8. [DOI: 10.1080/00015458.2015.11681129]
16. McGaw T, Elkins TE, DeLancey JO, McNeeley SG, Warren J. Assessment of intraperitoneal adhesion formation in a rat model: can a procoagulant substance prevent adhesions? Obstet Gynecol. 1988;71(5):774-8. [PMID: 3357666]
17. Oryan A, Tabatabaei Naeini A, Moshiri A, Mohammadalipour A, Tabandeh MR. Modulation of cutaneous wound healing by silymarin in rats. J Wound Care. 2012;21(9):457-64. [DOI: 10.12968/jowc.2012.21.9.457]
18. Karaca G, Amioğlu H, Pekcici MR, Demirci H. The effect of thymoquinone and platelet-rich plasma on intra-abdominal adhesions. Medicina. 2025;61(7):1119. [DOI: 10.3390/medicina61071119]
19. Karthik KK, Cheriyan BV, Rajeshkumar S, Gopalakrishnan M. A review on selenium nanoparticles and their biomedical applications. Biomedical Technology. 2024;6:61-74. [DOI: 10.1016/j.bmt.2023.12.001]
20. Rotruck JT, Pope AL, Ganther HE, Swanson AB, Hafeman DG, Hoekstra WG. Selenium: biochemical role as a component of glutathione peroxidase. Science. 1973;179(4073):588-90. [DOI: 10.1126/science.179.4073.588]
21. Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal Biochem. 1979;95(2):351-8. [DOI: 10.1016/0003-2697(79)90738-3]
22. Kuşaslan R, Ercan G, Ağcaoğlu O, Altınay S, Binboğa S, Altınel Y. A novel coenzyme-Q approach for the prevention of postsurgical adhesion. Turk J Surg. 2020;36(2):202-8. [DOI: 10.5578/turkjsurg.4398]
23. Ward BC, Panitch A. Abdominal adhesions: current and novel therapies. J Surg Res. 2011;165(1):91-111. [DOI: 10.1016/j.jss.2009.09.015]
24. Javdani M, Dourandish Y, Karimi Babaahmadi B, Balali Dehkordi S. Protective Effects of Tannic Acid–Loaded Selenium Nanoparticles against Peritoneal Adhesions via Regulating Oxidative Stress and Inflammatory Gene Expression. Vet Comp Biomed Res. 2026;3(2):61-70. [DOI: 10.22103/VCBR.2026.26578.1116]
25. Hosnedlova B, Kepinska M, Skalickova S, Fernandez C, Ruttkay-Nedecky B, Peng Q, et al. Nano-selenium and its nanomedicine applications: a critical review. Int J Nanomedicine. 2018;13:2107-28.

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[DOI: 10.2147/IJN.S157541]
26. Canbey Göret C, Kiraz A, Göret NE, Oğuz Kılıç S, Özkan ÖF, Karaayvaz M. The activity of topical coenzyme Q10 (ubiquinol) in burned rats: results from an experimental study. East J Med. 2019;24(1):80-5. [DOI: 10.5505/ejm.2019.66934]
27. Nair SK, Bhat IK, Aurora AL. Role of proteolytic enzyme in the prevention of postoperative intraperitoneal adhesions. Arch Surg. 1974;108(6):849-53. [DOI:10.1001/archsurg.1974.01350300081019]
28. Ten Broek RP, Issa Y, Van Santbrink EJ, Bouvy ND, Kruitwagen RF, Jeekel J, et al. Burden of adhesions in abdominal and pelvic surgery: systematic review and meta-analysis. BMJ. 2013;347:f5588. [DOI: 10.1136/bmj.f5588]
29. Teo ZY, Senthilkumar SD, Srinivasan DK. Nanotechnology-based therapies for preventing post-surgical adhesions. Pharmaceutics. 2025;17(3):389. [DOI: 10.3390/pharmaceutics17030389]
30. Zhang Y, Hu D, Zhang B, Tang X, Zeng S, Wang B, et al. Application of biomaterials for the prevention of postoperative adhesion. Mater Today Adv. 2026;30:100766. [DOI: 10.1016/j.mtadv.2026.100766]

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